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NEWS 12	MAY 01	New CAS web site launched
NEWS 13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS 15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS 16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS 17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS 18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19	JUN 18	CA/CAplus to be enhanced with pre-1967 CAS Registry Numbers

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

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=> file caplus

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FILE 'CAPLUS' ENTERED AT 08:52:41 ON 19 JUN 2007
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FILE COVERS 1907 - 19 Jun 2007 VOL 146 ISS 26
FILE LAST UPDATED: 17 Jun 2007 (20070617/ED)


```
=> s ?melanin
L1        11418 ?MELANIN

=> s antibod?
L2       493688 ANTIBOD?

=> s l1 (L) l2
L3          212 L1 (L) L2

=> s (cancer? or tumor? or neoplas? or melanom?)
         334731 CANCER?
         472663 TUMOR?
         497296 NEOPLAS?
          35511 MELANOM?
L4       791713 (CANCER? OR TUMOR? OR NEOPLAS? OR MELANOM?)

=> s l4 and l3
L5           62 L4 AND L3

=> s l5 not py>2002
       5382046 PY>2002
L6           49 L5 NOT PY>2002

=> d ibib abs kwic
```

L6 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:711229 CAPLUS <<LOGINID::20070619>>
DOCUMENT NUMBER: 136:4079
TITLE: Abnormal translocation of tyrosinase and tyrosinase-related protein 1 in cutaneous melanocytes of Hermansky-Pudlak syndrome and in melanoma cells transfected with anti-sense HPS1 cDNA
AUTHOR(S): Sarangarajan, Rangaprasad; Budev, Ashish; Zhao, Yang; Gahl, William A.; Boissy, Raymond E.
CORPORATE SOURCE: Department of Dermatology, University of Cincinnati, Cincinnati, OH, USA
SOURCE: Journal of Investigative Dermatology (2001), 117(3), 641-646
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hermansky-Pudlak syndrome is an autosomal recessive disorder characterized by oculocutaneous albinism, a bleeding disorder, and, in some patients, ceroid storage and progressive lung disease. Although Hermansky-Pudlak syndrome exhibits locus heterogeneity, most patients have mutations in the HPS1 gene. Melanocytes in the basal epithelial layer of skin from patients with different mutations in the HPS1 gene exhibited occasional large complexes containing dihydroxyphenylalanine-pos. cisterna and 50 nm

vesicles. To characterize the role of the HPS1 protein in cells, human HPS1 cDNA was transfected into pigmented SK-MEL-188 melanoma cells (M-188) in either the sense (S-188) or the antisense (A-188) orientation. Expression of the 79 kDa HPS1 protein (in M-188 and S-188 cells) or lack of expression (in A-188 cells) was confirmed by Western blotting using two HPS1-protein-specific polyclonal antibodies. Significant reduction in expression of HPS1 protein in A-188 cells resulted in a significant decrease in tyrosinase activity and melanin content compared with M-188 and S-188 cells using an intact cell assay for tyrosinase. In contrast, tyrosinase activities in cell lysates of M-188, S-188, and A-188 cells were not significantly different. Knockout of HPS1 protein expression in A-188 cells caused both tyrosinase and tyrosinase-related protein 1 to be localized to large granular complexes in the cell cytosol and dendrites. Electron microscope anal. of the A-188 cells revealed that absence of HPS1 protein resulted in the deposition of dihydroxyphenylalanine reaction products (i.e., tyrosinase) confined to large membrane-bound structures with limiting membranes. We conclude that lack of HPS1 protein expression results in mistranslocation of tyrosinase and tyrosinase-related protein 1 to large granular complexes rather than melanosomes, compromising melanin synthesis.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Abnormal translocation of tyrosinase and tyrosinase-related protein 1 in cutaneous melanocytes of Hermansky-Pudlak syndrome and in melanoma cells transfected with anti-sense HPS1 cDNA

AB Hermansky-Pudlak syndrome is an autosomal recessive disorder characterized by oculocutaneous albinism, a bleeding disorder, and, in some patients, ceroid storage and progressive lung disease. Although Hermansky-Pudlak syndrome exhibits locus heterogeneity, most patients have mutations in the HPS1 gene. Melanocytes in the basal epithelial layer of skin from patients with different mutations in the HPS1 gene exhibited occasional large complexes containing dihydroxyphenylalanine-pos. cisterna and 50 nm vesicles. To characterize the role of the HPS1 protein in cells, human HPS1 cDNA was transfected into pigmented SK-MEL-188 melanoma cells (M-188) in either the sense (S-188) or the antisense (A-188) orientation. Expression of the 79 kDa HPS1 protein (in M-188 and S-188 cells) or lack of expression (in A-188 cells) was confirmed by Western blotting using two HPS1-protein-specific polyclonal antibodies. Significant reduction in expression of HPS1 protein in A-188 cells resulted in a significant decrease in tyrosinase activity and melanin content compared with M-188 and S-188 cells using an intact cell assay for tyrosinase. In contrast, tyrosinase activities in cell lysates of M-188, S-188, and A-188 cells were not significantly different. Knockout of HPS1 protein expression in A-188 cells caused both tyrosinase and tyrosinase-related protein 1 to be localized to large granular complexes in the cell cytosol and dendrites. Electron microscope anal. of the A-188 cells revealed that absence of HPS1 protein resulted in the deposition of dihydroxyphenylalanine reaction products (i.e., tyrosinase) confined to large membrane-bound structures with limiting membranes. We conclude that lack of HPS1 protein expression results in mistranslocation of tyrosinase and tyrosinase-related protein 1 to large granular complexes rather than melanosomes, compromising melanin synthesis.

ST tyrosinase TRP1 translocation melanocyte Hermansky Pudlak syndrome; melanoma HPS1 tyrosinase related protein 1 translocation

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HPS1; abnormal translocation of tyrosinase and tyrosinase-related protein 1 in human cutaneous melanocytes of Hermansky-Pudlak syndrome and in melanoma cells transfected with anti-sense HPS1 cDNA)

IT Blood coagulation disorders
(Hermansky-Pudlak syndrome; abnormal translocation of tyrosinase and tyrosinase-related protein 1 in human cutaneous melanocytes of Hermansky-Pudlak syndrome and in melanoma cells transfected with anti-sense HPS1 cDNA)

```
IT   Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (TRP-1 (tyrosinase-related protein 1); abnormal translocation of
        tyrosinase and tyrosinase-related protein 1 in human cutaneous
        melanocytes of Hermansky-Pudlak syndrome and in melanoma
        cells transfected with anti-sense HPS1 cDNA)
IT   Albinism
     Human
       Melanoma
        (abnormal translocation of tyrosinase and tyrosinase-related protein 1
        in human cutaneous melanocytes of Hermansky-Pudlak syndrome and in
        melanoma cells transfected with anti-sense HPS1 cDNA)
IT   Melanins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (abnormal translocation of tyrosinase and tyrosinase-related protein 1
        in human cutaneous melanocytes of Hermansky-Pudlak syndrome and in
        melanoma cells transfected with anti-sense HPS1 cDNA)
IT   Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (gene HPS1; abnormal translocation of tyrosinase and tyrosinase-related
        protein 1 in human cutaneous melanocytes of Hermansky-Pudlak syndrome
        and in melanoma cells transfected with anti-sense HPS1 cDNA)
IT   Biological transport
        (intracellular; abnormal translocation of tyrosinase and
        tyrosinase-related protein 1 in human cutaneous melanocytes of
        Hermansky-Pudlak syndrome and in melanoma cells transfected
        with anti-sense HPS1 cDNA)
IT   59-92-7, DOPA, biological studies   9002-10-2, Tyrosinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (abnormal translocation of tyrosinase and tyrosinase-related protein 1
        in human cutaneous melanocytes of Hermansky-Pudlak syndrome and in
        melanoma cells transfected with anti-sense HPS1 cDNA)


=> s radiolab?
L7       39507 RADIOLAB?

=> s l7 and l6
L8           1 L7 AND L6

=> d ibib

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:       1985:486168  CAPLUS <<LOGINID::20070619>>
DOCUMENT NUMBER:        103:86168
TITLE:                  Pigmentation-associated glycoprotein of human
                        melanomas and melanocytes:  definition with a
                        mouse monoclonal antibody
AUTHOR(S):              Thomson, Timothy M.; Mattes, M. Jules; Roux, Linda;
                        Old, Lloyd J.; Lloyd, Kenneth O.
CORPORATE SOURCE:       Mem. Sloan-Kettering Cancer Cent., New York, NY,
                        10021, USA
SOURCE:                 Journal of Investigative Dermatology (1985), 85(2),
                        169-74
                        CODEN: JIDEAE; ISSN: 0022-202X
DOCUMENT TYPE:          Journal
LANGUAGE:               English


=> d ibib abs kwic

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:       1985:486168  CAPLUS <<LOGINID::20070619>>
DOCUMENT NUMBER:        103:86168
```

TITLE: Pigmentation-associated glycoprotein of human melanomas and melanocytes: definition with a mouse monoclonal antibody

AUTHOR(S): Thomson, Timothy M.; Mattes, M. Jules; Roux, Linda; Old, Lloyd J.; Lloyd, Kenneth O.

CORPORATE SOURCE: Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA

SOURCE: Journal of Investigative Dermatology (1985), 85(2), 169-74
CODEN: JIDEAE; ISSN: 0022-202X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pigmented melanoma cells and cultured melanocytes express a differentiation-related glycoprotein designated as pigmentation-associated antigen (PAA) of mol. weight 70,000-80,000. As described previously, PAA was initially defined by reactivity with antibodies in the serum of a patient with melanoma. The production and characterization of a mouse monoclonal antibody to PAA is described. This antibody (Ab TA99, and IgG2a) was shown by sequential immunopptn. expts. to react with the same component as the human antibody. Ab TA99 immunopptd. PAA from lysates of cells radiolabeled with [35S]methionine, [3H]glucosamine, [3H]fucose, and [3H]mannose as well as 125I. Using Ab TA99, the distribution of PAA was examined in frozen sections of 19 normal tissues and quant. in 68 tissue culture cell lines. In frozen sections, only melanin-containing cells were pos., including epithelial cells in the basal layer of the epidermis, in which pigment originates from melanocytes by transfer of melanosomes, and pigmented cells of the eye. In tissue culture cell lines, only pigmented melanoma cells were pos. PAA is an intracellular antigen, with a distribution very similar to that of melanosomes. This evidence confirms the close association of PAA with melanin production, and suggests that PAA may be a melanosome component. PAA was different from tyrosinase, the enzyme involved in melanin synthesis, but it was identical to the previously recognized glycoprotein, gp75, characteristic of pigmented melanomas and melanocytes.

TI Pigmentation-associated glycoprotein of human melanomas and melanocytes: definition with a mouse monoclonal antibody

AB Pigmented melanoma cells and cultured melanocytes express a differentiation-related glycoprotein designated as pigmentation-associated antigen (PAA) of mol. weight 70,000-80,000. As described previously, PAA was initially defined by reactivity with antibodies in the serum of a patient with melanoma. The production and characterization of a mouse monoclonal antibody to PAA is described. This antibody (Ab TA99, and IgG2a) was shown by sequential immunopptn. expts. to react with the same component as the human antibody. Ab TA99 immunopptd. PAA from lysates of cells radiolabeled with [35S]methionine, [3H]glucosamine, [3H]fucose, and [3H]mannose as well as 125I. Using Ab TA99, the distribution of PAA was examined in frozen sections of 19 normal tissues and quant. in 68 tissue culture cell lines. In frozen sections, only melanin-containing cells were pos., including epithelial cells in the basal layer of the epidermis, in which pigment originates from melanocytes by transfer of melanosomes, and pigmented cells of the eye. In tissue culture cell lines, only pigmented melanoma cells were pos. PAA is an intracellular antigen, with a distribution very similar to that of melanosomes. This evidence confirms the close association of PAA with melanin production, and suggests that PAA may be a melanosome component. PAA was different from tyrosinase, the enzyme involved in melanin synthesis, but it was identical to the previously recognized glycoprotein, gp75, characteristic of pigmented melanomas and melanocytes.

ST melanin pigmentation assocd antigen; melanoma pigmentation assocd antigen

IT Melanocyte
Melanoma

(pigmentation-associated antigen of, of human)
IT Antigens
RL: BIOL (Biological study)
(pigmentation-associated, of melanin-containing cells and melanoma, of human)

=> d his

(FILE 'HOME' ENTERED AT 08:52:02 ON 19 JUN 2007)

FILE 'CAPLUS' ENTERED AT 08:52:41 ON 19 JUN 2007
L1 11418 S ?MELANIN
L2 493688 S ANTIBOD?
L3 212 S L1 (L) L2
L4 791713 S (CANCER? OR TUMOR? OR NEOPLAS? OR MELANOM?)
L5 62 S L4 AND L3
L6 49 S L5 NOT PY>2002
L7 39507 S RADIOLAB?
L8 1 S L7 AND L6

=> file pctfull
COST IN U.S. DOLLARS SINCE FILE ENTRY 25.95 TOTAL SESSION 26.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY -1.56 TOTAL SESSION -1.56

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FILE LAST UPDATED: 18 JUN 2007 <20070618/UP>
MOST RECENT UPDATE WEEK: 200724 <200724/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s ?melanin
L9 3732 ?MELANIN

=> s antibod?
L10 98997 ANTIBOD?

=> s l9 (S) l10
L11 173 L9 (S) L10

=> d kwic

L11 ANSWER 1 OF 173 PCTFULL COPYRIGHT 2007 Univentio on STN

DETD . . . or more of a 5-HT
(serotonin) transporter inhibitor, a NE (norepinephrine) transporter inhibitor, a CB-1 (can-
nabinoid-1 receptor) antagonist/inverse agonist, a ghrelin antibody, a ghrelin antagonist, a
H3 (histamine 1-13) antagonist/inverse agonist, a MCM R (melanin concentrating hormone
R) antagonist, a MCH2R (melanin concentrating hormone 2R) agonist/antagonist, a
NPY1 (neuropeptide Y Y1) antagonist, a NPY2 (neuropeptide Y Y2) agonist, a NPY5
lo (neuropeptide Y Y5). . .

```
=> s (cancer? or tumor? or neoplas? or melanom?)
         89387 CANCER?
         74135 TUMOR?
         25951 NEOPLAS?
         22854 MELANOM?
L12     111614 (CANCER? OR TUMOR? OR NEOPLAS? OR MELANOM?)

=> s l12 and l11
L13        161 L12 AND L11

=> s l13 not py>2002
        554496 PY>2002
L14         58 L13 NOT PY>2002

=> d kwic

L14    ANSWER 1 OF 58    PCTFULL   COPYRIGHT 2007 Univentio on STN

DETD  . . . disturbances associated with obesity, the metabolic syndrome X,
      anorexia, wasting disorders associated with chronic diseases, metabolic
      disorders,
      diabetes, obesity, infectious disease, anorexia, cancer
      -associated cachexia, cancer,
      neurodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder,
      immune
      disorders, and hematopoietic disorders, or other disorders related to
      cell signal processing
      and metabolic pathway modulation.. . .

      For example, the compositions of the present invention will have
      efficacy for
      treatment of patients suffering from: Cancer including
      pancreatic cancer, adenoma, brain
        tumor, colon cancer breast cancer,
      prostate cancer, testis cancer, neurological
      disorders
      including age-related disorders, Alzheimer's disease, Stroke,
      Parkinson's disease,
      Huntington's disease, Cerebral palsy, Epilepsy, Behavioral disorders,
      Addiction, Anxiety,
      Pain, nephropathy, neurodegenerative disorders,. . .
  . . .
      need thereof. By
      way of nonlimiting example, the compositions of the present invention
      will have efficacy
      for treatment of patients suffering from Cancer including
      pancreatic cancer, adenorna,
      brain tumor, colon cancer breast cancer,
      prostate cancer, testis caricer, neurological
      disorders including age-related disorders, Alzheimer's disease, Stroke,
      Parkinson's disease,
      Huntington's disease, Cerebral palsy, Epilepsy, Behavioral disorders,
      Addiction, Anxiety,
      Pain, nephropathy,. . .

      The invention further includes a method for screening for a modulator of
      disorders
      or syndromes including, e.g., Cancer including pancreatic
      cancer, adenoma, brain tumor,
      colon cancer breast cancer, prostate cancer
      , testis cancer, neurological disorders including
      age-related disorders, Alzheimer's disease, Stroke, Parkinson's disease,
```

Huntington's
disease, Cerebral palsy, Epilepsy, Behavioral disorders, Addiction, Anxiety, Pain,
nephropathy, neurodegenerative disorders,. . .
. . .
is a method for screening for a modulator of
activity, or of latency or predisposition to an disorders or syndromes including, e.g.,
Cancer including pancreatic cancer, adenoma, brain
tumor, colon cancer breast cancer,
prostate cancer, testis cancer, neurological
disorders including age-related disorders,
Alzheimer's disease, Stroke, Parkinson's disease, Huntington's disease, Cerebral palsy,
Epilepsy, Behavioral disorders, Addiction, Anxiety, Pain, nephropathy, neurodegenerative
disorders,. . .
. . .
disturbances associated with obesity, the metabolic syndrome X,
anorexia, wasting disorders associated with chronic diseases, metabolic disorders
diabetes, obesity, infectious disease, anorexia, cancer
-associated cachexia, cancer,
ne-urodegenerative disorders, Alzheimer's Disease, Parkinson's Disorder, immune
disorders, and hernatopoietic disorders. Also, the expression levels of the new
polypeptides of the invention can be used in a method to screen for various cancers as well
as to determine the stage of cancers.
. . .
a human subject), in an amount sufficient to alleviate or prevent the pathological condition. In preferred embodiments, the disorder, includes, e.g., Cancer
including pancreatic cancer, adenoma, brain tumor,
colon cancer breast cancer, prostate
cancer, testis cancer, neurological disorders
including age-related disorders, Alzheimer's
disease, Stroke, Park-inson's disease, Huntington's disease, Cerebral palsy, Epilepsy,
Behavioral disorders, Addiction, Anxiety, Pain, nephropathy, neurodegenerative. . .

The nucleic acids and proteins of the invention are useftil in potential therapeutic
applications implicated in pancreatic cancer, adenoma, and
other cancers, Larsen
syndrome, tachycardia, erythroderma, night blindness, long QT syndrome, brugada
syndrome, heart block, cell-mediated immunity, and applications as a mediator in
5 inflammation. . . thereof By way of
nonlimiting example, the compositions of the present invention will have efficacy for
treatment of patients suffering from pancreatic cancer,
adenonia, and other cancers, Larsen
syndrome, tachycardia, erythroderma, night blindness, long QT syndrome, brugada
syndrome, heart block, cell-mediated immunity, and applications as a mediator in
inflammation. The. . .
. . .
Expec
Identifier organism (aa) (26) (o-o) t

PatP:B65663 Protein 1649 1626/1662 1632/1662 0.0
kinase [Homo 9 7 -o6 (98%)
sapiens]
PatP:B43S81 Cancer 604 592/609 594/609 6.5e-
associated (97o-,) (97%) 3 06
protein [Homo
sapiens]
PatP:B42761 ORF2525 619 585/624 s9G/624 1.3e-
polypeptide (93%) (95%) 3 00
gij107641G5jgbjAAG225 GCN2gamma 15. . .

68
It was found that transforming growth factor-betal acts as a potent inhibitor of
complement C3 biosynthesis in human pancreatic cancer cell lines. Andoh et al.

determined how transforming growth factor (TGF)-betal affects complement O secretion
in the pancreatic cancer cell lines PANC-1 and BxPC It is suggested that TGF-betal
may act as a potent inhibitor of C3 secretion in pancreatic cancer cell lines under
inflammatory conditions. This action of TGF-betal did not correlate with NF-kappaB
activation, but associated with the translocation of Fos. . .

. . .
Therefore, the nucleic acid and protein of the
invention are useful in potential therapeutic applications implicated, for example but not
limited to, cancer, lung diseases, including asthma, immundeficiencies, inflammation,
Crohds disease, neurological disorders, nephropathy, and other diseases and disorders.

. . .
antigenic secreted and membrane proteins suggests that antibodies directed against the novel genes may be useful in treatment and prevention of cancer, lung
diseases, including asthma, immundeficiencies, inflammation, Crohn's disease,
neurological disorders, nephropathy, and other diseases and disorders.

The nucleic acids and proteins of the invention are useful in potential therapeutic
applications implicated in cancer, lung diseases, including asthma, immundeficiencies,
inflammation, Crohn's disease, neurological disorders, nephropathy, and other diseases
and disorders. For example, but not limited to,. . . the compositions of the present invention will have efficacy for treatment of
patients suffering from, for example, but not limited to, cancer , lung diseases, including
asthma, immundeficiencies, inflammation, Crohn's disease, neurological disorders,
nephropathy, and other diseases and disorders. The novel nucleic acid encoding the. . .

. . .
cell polarity, and the establishment of cell fates. Wntl was identified as an
oncogene activated by the insertion of mouse mammary tumor virus in virus-induced
mammary adenocarcinomas. Although Wntl is not expressed in the normal mammary
gland, expression of Wntl in transgenic mice causes mammary

tumors. To identify downstream genes in the WNT signaling pathway that are relevant to the transformed cell I 0 phenotype, A PCR-based cDNA. . . distinct systems demonstrated WISP 5 induction to be associated with the expression of)VNTl. WISP 1 genomic DNA was amplified in colon cancer cell lines and in h-uman colon tumors and its RNA overexpressed in 84% of the tumors examined compared with patient-matched normal mucosa. WISP3 also was overexpressed in 63% of colon tumors analyzed. In contrast, WISP2 showed reduced RNA expression in 79% of the tumors. These results suggested that WISP genes may be downstream of WNT1 signaling and that aberrant levels of WISP expression in colon cancer may play a role in colon tumorigenesis.

The nucleic acids and proteins of the invention are useful in potential therapeutic applications implicated in neurodegenerative disorders, epilepsy, cancers including but not limited to brain tumor, colon cancer and breast cancer, developmental disorders, neural tube defects, and/or other pathologies and disorders. For example, a cDNA encoding the Writ 8-like protein may be useful. . . way of nonlimiting example, the compositions of the present invention will have efficacy for treatment of patients suffering from neurodegenerative disorders, epilepsy, cancers including but not limited to brain tumor, colon cancer and breast cancer, developmental disorders, and neural tube defects,. The novel nucleic acid encoding Writ 8-like protein, and the Wnt 8- like protein of the. . .

It was stated that prostate carcinoma is the most prevalent form of cancer in males and the second leading cause of cancer death among older males. The use of the serum prostate-specific antigen test permits early detection of human prostate cancer; however, early detection has not been accompanied by an improvement in determining which tumors may progress to the metastatic stage. The process of tumor metastasis is a multistage event involving local invasion and destruction of extracellular matrix; intravasation into blood vessels, lymphatics or other channels of. . . into the secondary site; and growth in the new location. Common to many components of the metastatic process is the requirement for tumor cell motility. A well-characterized series of cell lines that showed varying 84 metastatic potential was developed from the Dunning rat prostate carcinoma.. . . 1 5 by them, was found to deregulate motility in prostate cells directly. In addition, it was expressed in advanced human prostate cancer specimens, but not in normal human prostate or benign

prostatic hyperplasia,
suggesting its potential use as a new marker for prostate. . .

1 0 (I 996) found that thymosin-beta- 1 5 levels correlated positively with the Gleason tumor
grade. Coffey (I 996) pointed out that the upregulation of thymosin-beta- 1 5 as a positive
motility factor and the down regulation. . .

The nucleic acids and proteins of the invention are useful in potential therapeutic
applications implicated in cancer including but not limited to prostate cancer,
immunological and a-Litoimmune disorders (i.e., hyperthyroidism), angiogenesis and MOL6
MOL6a
The disclosed novel Trypsin-like MOL6a nucleic acid of 730 nucleotides (also
referred to as. . .
. .
useful in potential therapeutic
applications implicated in failure to thrive, nutritional edema, and hypoproteinemia,
trypsinogen deficiency disease, chronic and heriditary pancreatitis, enterkinase
defieciency, cancer and/or related pathologies and disorders and/or other pathologies and
disorders. For example, a cDNA encoding the Trypsin-like protein may be useful. . . for treatment of patients suffering from fail-Lire to thrive, nutritional edema,
and hypoproteinemia, trypsinogen deficiency disease, chronic and heriditary pancreatitis,
enterkinase defieciency, cancer. The novel nucleic acid encoding Trypsin-like protein,
and the Trypsin-like protein of the invention, or fragments thereof, may further be useful
in. . .
. .
or prostate-
specific antigen (PSA). The latter two genes are almost prostate-specific and they are used
for diagnosis and monitoring of prostate cancer and more recently, in breast cancer
applications (Yousef et aL, Anticancer Res 1999 Jul-Aug;19(413):28431-52). These new
genes, like the already known kallikreins, may have utility for diagnosis, monitoring and
therapeutics of various cancers including those of the breast, prostate and testis.
. .
the nucleic acid and protein of
the invention are useful in potential therapeutic applications implicated, for example but
not limited to, various cancers including those of the testis, prostate, and breast;
mammalian reproduction, especially spermatogenesis; blood pressure regulation; and other
diseases and disorders. The homology. . . antigenic secreted and membrane proteins
suggests that antibodies directed against the novel genes may be useful in treatment and
prevention of various cancers including those of the testis, prostate, and breast;
mammalian reproduction, especially spermatogenesis; blood pressure

regulation; and other
diseases and disorders.

The nucleic acids and proteins of the invention are useful in potential therapeutic
applications implicated in various cancers including those of the testis, prostate, and
breast; mammalian reproduction, especially spermatogenesis; blood pressure
regulation;and other diseases and disorders. For example, but. . . the compositions of the present
invention will have efficacy for treatment of patients suffering from, for example, but not
limited to, various cancers including those of the testis, prostate, and breast; mammalian
reproduction, especially spermatogenesis; blood pressure regulation; and other diseases
101
and disorders. The novel. . .

. . .
is expressed in'the following tissues: fetal thymus, mammary gland, fetal
thymus, pool of ten tissues (adrenal, mammary, prostate, testis, uterus, bone marrow*,
melanoma*, pituitary*, thyroid*, spleen) (*from mRNA rather than from total RNA).

Tissue expression
MOL8 is expressed in at least the following tissues: kidney, senescent fibroblasts,
lymphocyte, B cell, and germ cell tumors. Expression information was derived from the
tissue sources of the sequences that were included in the derivation of the sequence of
CuraGen. . .

108
The nucleic acids and proteins of the invention are useful in potential therapeutic
applications implicated in various cancers including those metabolic disorders, e.g.

. . .
the
compositions of the present invention will have efficacy for treatment of patients suffering
from, for example, but not limited to, various cancers including those of the metabolic
disorders, e.g. Hypercholesterolemia, viral diseases, and other diseases and disorders. The
novel nucleic acid encoding the novel. . .

. . .
least the following tissues: fetal lung, testis, B-cell,
aorta, brain, colon, foreskin, germ cell, heart, kidney, pancreas, stomach, uterus, whole
embryo and cancer cell lines MDA-MB-231 and MCF
These materials are further useful in the generation of antibodies that bind
immuno-specifically to the novel. . .

. . .
endopeptidase and 17 matching the corresponding segment of pig-
soluble angiotensin 11-binding protein. Moreover, the rat protein is recognized by a
monoclonal antibody against rabbit soluble angiotensin
11-binding protein, all of which is

consistent with these proteins being species variants of a single protein. . . schizophrenics and age- and sex-matched controls. Neurotensin/neuromedin N messenger RNA was observed in ventral mesencephalic cells some of which also contained melanin pigment or tyrosine hydroxylase messenger RNA. Neurons expressing neurotensin/neuromedin N messenger RNA were observed in the ventral mesencephalon of both schizophrenic and. . .

. . .

need thereof. By way of nonlimiting example, the compositions of the present invention will have efficacy for treatment of patients suffering from Cancer, Trauma, Viral/bacterial/parasitic infections, Cardiomyopathy, Atherosclerosis, Hypertension, Congenital heart defects, Aortic stenosis, Atrial septal defect (ASD), Atrioventricular (A-V) canal defect, Ductus arteriosus, Pulmonary stenosis,. . .

. . .

related compounds according to the invention will be I 3 4 useful in therapeutic and diagnostic applications in proliferative and apoptotic disorders, e.g. cancer, Alzheimer's disease, and obesity.

cancer and ischemic injury.

. . .

the treatment and/or diagnosis of a variety of diseases and pathologies, including by way of nonlimiting example, those involving psoriatic skin and cancer , e.g. basal and squamous cell carcinomas.

Insulin-like growth factor proteins are associated with cancer progression. The down-regulation of T I A I 2/mac2 5, a novel insulin-like growth factor binding-like protein related gene, is associated with disease progression in breast carcinomas. To define genes that are essential to the initiation and progression of breast cancer Burger and colleagues 3 0 utilized subtractive hybridization and differential display cloning techniques and isolated over 950 cDNAs from breast cell-lines derived from matched normal and tumor tissue. Of these, 102 cDNAs were characterized by DNA sequencing and Northern blot analysis.

Microsatellite length polymorphism was studied using markers for 4q in paired normal and tumor breast tissues. Thirty-three per cent (I 0/3 0) of the samples were found to be polymorphic with D4S 1 8 9. . . markers and LOH was detected in 50% (5110) of these informative samples. The data indicate that T1AI2/mac25 expression is abrogated during breast cancer progression concomitant with loss of heterozygosity on chromosome 4q. T IA I 2/mac25 may therefore have a tumor suppressor-like function and its expression could indicate a disease with a more favorable status',

having a better
prognosis (See Burger et aL,. . .
. . .
al. provide evidence from genetic and pharinacologic studies to suggest that cyclooxygenase-2 (COX-2) enzyme plays a role in the development of colorectal
cancer (Gupta et al., PNAS 97(24): 13275-80, November 21, 2000. However, little is
known about the identity or role of the eicosanoid. . . mouse uterus via activation of the nuclear hormone
receptor peroxisome proliferator-activated receptor (PPAR) delta. Analysis of PPARdelta
mRNA in matched normal and tumor samples revealed that, similar to COX-2, the
expression of PPARdelta is upregulated in colorectal carcinomas (Ld.). Moreover, mRNA
of both COX-2 and PPARdelta localize to the same region within a tumor. Transfection
assays indicate that endogenously synthesized prostacyclin (PGI(2)) can serve as a ligand
for PPARdelta. Carbaprostacyclin, a stable PGI(2) analog and a. . . of endogenous PPARdelta in human
colon carcinoma cells. Thus, it appears that PPARdelta behaves similarly to COX-2, is
aberrantly expressed in colorectal tumors, and is transcriptionally responsive to PGI(2).
. . .
treatment and/or diagnosis of a variety of diseases and pathologies, including by way of nonlimiting example, those involving cell proliferative
disorders, e.g. cancer.
. . .
have also been
categorized according to other aspects, such as family history, age, course of disease, or
presence of a concomitant myeloid neoplasm. However, so far, generally accepted disease
criteria are missing. Recently, a number of diagnostic (disease-related) markers have been
identified in mastocytosis research.. . . mast cell enzyme tryptase is
increasingly used as a serum- and immunohistochemical marker to estimate the actual
spread of disease (burden of neoplastic mast cells). The clinical significance of novel
mastocytosis markers is currently under investigation. First results indicate that they may
be useful to. . .

By subtractive hybridization, Schweinfest and co-workers isolated a cDNA for a tumor
suppressor candidate gene, which they called DRA (downregulated in adenoma), from a
normal colon tissue cDNA library. Its expression, which appeared to. .
. . .
a
variety of diseases and pathologies, including by way of nonlimiting example, those
1)0
involving disorders such as Pendred syndrome, skeletal dysplasias, diastrophic dysplasia,
cancer, adenoma.
. . .

cultured broth as a low
molecular weight inhibitor of cell adhesion to extracellular matrix
(ECM), has anti-
metastatic activity against B 16 melanoma cells in vivo.
Inhibition of cell adhesion to ECM
168
by cytostatin has been evaluated (See Kawada et al., 1999, Biochim.
Biophys.. . .
. . .
apoptosis
inducer- bactobolin has been analyzed. Since, most solid turnor cells
are less sensitive to
apoptosis induced by anticancer drugs than hematopoietic cancer
cells, Kawada and co- WO 02/102321 PCT/US02/19522
polypeptide can be used amongst other things to modulate breast
development and milk
production. The. . .
. . .
of diseases and pathologies, including by way of nonlimiting
example, those involving disorders characterized by altered cell shape,
motility, and
apoptosis, e.g. cancer and ischemic injury.
. . .
Pathologies that are blocked by the use of MOL20 and 21 antibodies
include metastatic
176
potential and invasion in kidney and gastric tumors; cell
growth and cell survival in colon,
breast, liver and gastric tumors; cell growth and cell
survival in colon, breast, liver and
gastric turnors; metastasis in breast and brain tumors;
metastasis and chemotherapy
resistance in colon, gastric, ovarian and lung tumors; and
angiogenesis and tumor growth
in liver cancer.
. . .
in Table 22B. Also, a MOL22 polypeptide has a
high degree of homology (94% identity, 97% similarity) with a human lung
tumor-specific
antigen polypeptide (HLTA; PatP Accession No.: B44409), as is shown in
Table 22C.
. . .
4: 72) and the EBV hybridoma technique to produce human
monoclonal antibodies (see, e.g, Cole, et aL, 1985. In: MONOCLONAL
ANTIBODIES AND
CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human
monoclonal antibodies may be
utilized in the practice of the invention and may. . .

MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc.,
pp. 77-96). Each of
the above citations is incorporated herein by reference in their
entirety.

214-218; Nishimura, et al., 1987. Cancer Res. 47: 999-1005;
Wood, et al., 1985. Nature
314 :446-449; Shaw, et al., 1988. J Natl. Cancer Inst. 80:
1553-1559); Morrison(1985)
Science 229:1202-1207; Oi, et al. (I 986) BioTechniques 4:214; Jones, et
al., 1986. Nature
3)21: 552-525; Verhoeyan,. . .
. . .
metabolic disturbances
associated with obesity, the metabolic syndrome X as well as anorexia

and wasting
disorders associated with chronic diseases and various cancers
, and infectious
disease(possesses anti-microbial activity) and the various
dyslipidemias. In addition, the
anti-MOLX antibodies of the invention can be used to detect. . .
<------User Break------>

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.40	33.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.56

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